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EDITORIAL

In this issue of the Journal there are two articles which we think should claim the interest and, maybe, comment of all our readers.

One article deals with the value of the tuberculin test, in this particular instance as it may be interpreted in the case of cattle affected by extensive lesions. Probably no diagnostic test has been subjected to more criticism on the one hand and on the other hand to more commendation, and at times it has been difficult to draw the line between these two extremes. Especially has this been so in the case of lay persons, who can only form their opinions on information which may be transmitted to them by those who one presumes are qualified to speak with authority. Mr. Doyle's article comes, therefore, at an opportune time. There can be no doubt as to its value, for the author has gone to considerable pains to delve into the literature on the subject and also to put the matter to a practical test. In his case, only one animal out of twenty-five clinically affected with tuberculosis failed to react to the tuberculin test. We agree with the author that on these figures it would appear that the tuberculin test has on many occasions been unfairly criticised. If the test had shown the percentage of inaccuracy which some would have us believe, we doubt whether the wonderful results which have been achieved in eradicating the disease in certain areas in America could have been accomplished.

In a second article, we have an author greatly distinguished in the agricultural field—Sir Albert Howard. We are sure that his article, which is headed "A New Policy for Veterinary Science," will be read with great interest by all veterinary surgeons. There is no doubt that much illness and disease could be avoided if we knew more about animal nutrition and the factors upon which good nutrition depended. It must have been evident to all thoughtful people, even in the early days of agriculture, that good stock depended upon good farming, and that where there was good farming there was a minimum of disease and animals could be brought to a state of maturity in a much shorter time. To some, Sir Albert Howard's ideas may be new, others may contest them, but they warrant the most careful consideration from all.

General Articles

THE VALUE OF THE TUBERCULIN TEST IN CATTLE AFFECTED WITH EXTENSIVE LESIONS OF TUBERCULOSIS

By T. M. DOYLE,
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THERE would appear to be some difference of opinion as to the extent to which cattle affected with extensive lesions of tuberculosis fail to react to the tuberculin test; therefore, before presenting the results of some tests carried out at this laboratory, it was thought worth while giving a fairly full review of the results obtained by other workers. Rodgers (1918) made post-mortem examinations of thirteen non-reactor cows, four showed lesions of tuberculosis and in two of these the lesions were extensive. Turner (1920) stated:

> "Some interesting points were brought out in compiling these tables, one of which seems to refute the generally accepted opinion that advanced cases of tuberculosis do not always react to the tuberculin test. We found that all of the generalised cases [39] had reacted to the original tests as well as to the seven-day retest."

O'Rear (1934), of the Tuberculosis Eradication Division, Bureau of Animal Industry, U.S.A., tested 305 cows in several heavily infected herds, using synthetic medium tuberculin in the caudal fold and reading the results at the 72nd hour. Two hundred and seventy-three animals gave positive reactions. Both positive and negative animals were submitted to post-mortem examination within ten days of testing. Thirty were found to have generalised tuberculosis and in each instance a positive reaction to the test had been obtained.

Calmette (1936) believed that animals with extensive lesions of the disease, and particularly those that are emaciated, do not generally react to tuberculin. Mohler (1938) stated:

> "Some critics of the tuberculin test have asserted that it does not detect badly diseased animals. On the contrary, official post-mortem evidence shows that tuberculin does detect badly infected tuberculous animals in the great majority of cases. In the earlier period of eradication work in the United States about 10 per cent. of reactors to the tuberculin test showed well-advanced lesions."

In a report of the Council for Scientific and Industrial Research, Australia (1939-40), it is stated that:

> "In any scheme to eradicate tuberculosis from cattle, a serious handicap is that many advanced cases of infection no longer react to the tuberculin test."

Bazeley and Barraclough (1940), during the course of routine examination of dairy herds in Australia, carried out a series of comparative tuberculin tests

on 1,595 cows using three tuberculins (H.8, H.9, D and H.T.75) prepared by the Commonwealth Serum Laboratories, two tuberculins (683 and 707) from the Bureau of Animal Industry, U.S.A., and one tuberculin (serial F) from the Health of Animals Branch, Canada.

The animals were divided into six groups, varying in number from 164 to 481; each group was tested with two tuberculins, one C.S.L. and one imported product, and both tuberculins were injected in the same caudal fold in doses of 0.05 c.c. All positive and doubtful reactors were submitted to post-mortem examination. Fifty-one cases of generalised infection were encountered and forty-eight of these gave positive reactions with either or both tuberculins. Three gave small reactions and were classified as doubtful (retest), but in the light of information subsequently obtained at post-mortem examinations, and the high incidence of tuberculosis in the herds, the authors finally considered small reactions as indicating infection. A total of 39 small reactions occurred and 14 of these were in cases of generalised infection. A typical example of a small reaction was one in which the caudal fold was one and a half times its normal thickness and contained a swelling half an inch in diameter.

The principal point of interest in the extensive investigations of Bazeley and Barraclough to the subject under discussion is that 48 out of 51 (94 per cent.) cases of generalised infection gave positive reactions to the tuberculin test and the remaining three were regarded as doubtful.

Legg and Maunder (1940) in Australia tested 865 "culled" dairy cows of various types and ages with synthetic medium tuberculin given as a single injection (0.05 c.c.) in the caudal fold. The animals were divided into three groups of 338, 256 and 271, respectively. The test of the first group was unsatisfactory, as a considerable number of non-reactors showed lesions on autopsy. There were six cases of generalised infection, four of which gave good reactions. In the fifth there was a small indefinite reaction at the 72nd hour, but as it had disappeared by the 96th hour it was regarded as negative. The sixth animal (C.40) showed no reaction.

In the second group, comprising 256 animals, the results were again unsatisfactory, as eight animals out of 231 regarded as negative were found on autopsy to be tuberculous. In this group seven cases of generalised infection occurred; three gave positive reactions at the 72nd hour, two more were positive at the 96th hour, the sixth animal gave a small indefinite reaction at the 96th hour, while the seventh animal showed no reaction.

It should be noted that a synthetic medium tuberculin (C.S.L.-H.8), concentrated by ultra-filtration, was used in testing these two groups. This is presumably the same tuberculin that was found by Bazeley and Barraclough (1940) to be of low potency. Evidence supporting this view was the tendency to "delayed reactions" and the suggestion of Legg and Maunder that if one reading only were to be practised, it should be at the 96th hour.

In the third group, comprising 271 animals, three tuberculins were used. Six cases of generalised infection occurred and as all were detected by one of the tuberculins (C.S.L.-H.9) it is unnecessary to give further details.

Legg and Maunder (1940) in a second report gave the results of tests on a further 453 cows. Two tuberculins, DH.1 and DH.1-2,* prepared by the Commonwealth Serum Laboratories, were used.

Lesions of tuberculosis were found on autopsy in 94 per cent. of reactors. Twelve animals were considered to have given doubtful reactions and five of these showed lesions on autopsy. In referring to these animals the authors state that "the reactions merely consisted of a small diffuse swelling of the caudal fold, present at either one or both readings." One (Q.30) of the five was a case of generalised infection and two others (V.7 and V.17) showed extensive lesions.

The reactions shown by these animals were described as follows:

"Q.30, caudal fold thickened, posterior portion hard and diffuse" (72nd hour);

"V.7, almond, hard, diffuse, looks like trauma" (96th hour);

"V.17, just appreciable thickening of caudal fold (72nd hour); similar, too hard" (96th hours).

From the description of the reactions shown, and in view of the heavy infection in the herds from which these animals came, they might reasonably have been regarded as infected at the time of testing.

In a later test, one animal (A.B.25) was considered to have given a doubtful reaction, described as a "small diffuse swelling of the fold over an area around the point of injection about 2 x 1 cm. at both readings." This animal was found to be affected with generalised tuberculosis. Here again the reaction would appear to have justified a positive diagnosis.

The significance of small reactions depends mainly on the incidence of tuberculosis in the particular herd; in a moderately or heavily infected herd the small reaction should be regarded as signifying infection; but when one or two small reactions occur in an otherwise clean herd the particular animals should be retested. Animals with advanced lesions of the disease or with old calcified lesions tend as a general rule to show small reactions to the test.

Legg and Maunder (1941) reported a further series of tests on 458 cows, using a synthetic medium tuberculin concentrated by ultra-filtration (C.S.L. H.9-2). It was given as a single injection (0.05 c.c.) in the caudal fold.

In this series, forty-two animals showed tuberculous lesions on autopsy. Amongst these were ten which had "extensive and widespread lesions throughout the body." Four of these showed no reaction to the test, and a fifth exhibited a small swelling at the 72nd hour. Four of the remainder were positive and one classed as doubtful showed a small indefinite swelling of the fold at the 72nd hour.

The reports by Legg and Maunder on their investigations leave the impression that they were rather hesitant in condemning animals exhibiting small

* The tuberculins DH.1 and DH.1-2 used by Legg and Maunder, and D and HT.75 mentioned by Bazeley and Barraclough (1940), were reported by Morgan and Garnet (1940) (Commonwealth Serum Laboratories) to be from the same batch of tuberculin issued under three separate batch numbers.

reactions, and more especially as they were dealing with cattle in which there was a high incidence of infection. They state, in regard to one group of animals: "The ten remaining animals presented swellings of the caudal fold, often quite large, but which we regarded as non-typical." They have, nevertheless, made a noteworthy contribution to an important aspect of the tuberculin test.

D'Arcy Hart (1932), in an investigation on the value of the tuberculin test in man, found that the error in negative reactions to the intracutaneous test, using O.T. in suitable doses, to be from 2 to 4 per cent.

Present Inquiry

In the course of an investigation carried out here an opportunity occurred to tuberculin test a number of cows removed from herds, under the Tuberculosis Order of 1925 (amended in 1938).

Most of the animals were in poor condition, many were emaciated, several were slaughtered *in extremis* on arrival at the laboratory and a few died of tuberculosis shortly after arrival. All were advanced cases of the disease, diagnosis being based in some cases on sputum or milk examination and in others on physical examination alone.

Three tuberculins were used in testing; these were Cambridge synthetic medium tuberculin, U.S.A. Bureau of Animal Industry synthetic medium tuberculin, and a broth tuberculin prepared by a commercial laboratory. The injections were made intradermally in the neck in a dose of 0.1 c.c. The B.A.I. tuberculin was given as a single injection, the other two tuberculins were used in either single or double injections according to the reaction exhibited at the 48th hour by the particular animal.

Twenty-five animals were tested and 24 of these gave positive reactions. One animal (668), tested with one tuberculin only, failed to react. A second animal (664) tested with two tuberculins on opposite sides of the neck, gave no reaction with one tuberculin, but reacted to the other. Nos. 660 and 662 were both tested with the three tuberculins and reacted to each of them. Eighteen of the positive animals were retested after periods varying from six to fifty days and again all gave positive reactions.

It was possible to submit only eleven animals to post-mortem examination (see Table), but three others were positive on sputum examination and two were positive udder cases; the clinical condition of the remaining nine animals, and the fact that they reacted to tuberculin, leaves no reasonable doubt that they were advanced cases of the disease.

Discussion

In considering this question it has to be borne in mind that great progress has been made during the last decade in the preparation and use of tuberculin. The potency has been raised and the uniformity of brews improved as shown by biological and chemical tests. The belief that many cattle affected with extensive lesions of tuberculosis are anergic dates back to the early days of testing, when the tuberculin available left much to be desired. For example,

Dorset (1934) reported that in comparative tests between broth and synthetic medium tuberculin carried out on 13,288 cattle, 1,127 reacted to the broth tuberculin and 1,268 to the synthetic medium tuberculin—a difference of approximately 11 per cent. One hundred and thirty-five of the 141 additional animals that reacted to synthetic tuberculin were found at autopsy to be tuberculous. No animal in the series reacted to broth tuberculin without at the same time reacting to the synthetic medium tuberculin.

The governing factors in the tuberculin test are the reliability of the tuberculin used, and the degree of allergy of the infected animal.

It is doubtful if much room remains for improvement in the best tuberculins as now prepared and obviously nothing can be done as regards the anergic state of certain animals; fortunately, the majority of these are of small value, being aged and in poor condition. It would appear, therefore, that with highly efficient modern tuberculin only an occasional animal, with extensive lesions of the disease, will fail to react to the test. This failure should not be attributed to the tuberculin, but to the state of the system of the particular animal.

Summary

One animal only out of twenty-five clinically affected with tuberculosis failed to react to the tuberculin test.

The frequency with which cattle affected with extensive lesions of tuberculosis fail to react to modern synthetic medium tuberculin is much overstated. Anergic animals undoubtedly occur but the number is small; and experience in America has proved that their presence has little influence on the eradication of the disease. They are usually aged and emaciated, facts that single them out for clinical examination.

Acknowledgment

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Summary of Tuberculin Tests—See Opposite

SUMMARY OF TUBERCULIN TESTS

No. of Cow	*First Test* PI 48 72	Result	Interval between 1st & 2nd test. Days	*Second Test* PI 48 72	Result	Condition of Animal	Post-mortem
677	6 9*15	Positive	7	6 10*16	Positive	Fair	Not done
674	5 14 13	„	7	5 13 11	„	Poor	„ „
694	5 18*28	„					
	5 18 22	„	16	6 13 21	„	Poor (T.B. lungs)	„ „
669	6 6*16	„	—	—	—	Emaciated	Extensive lesions in udder and mesenteric glands
672	5 11*20	„	—	—	—	Poor	Generalised
657	6 24 19	„	50	6 15 12	Positive	Emaciated Died 3 months after 1st test	„
656	6 27 27	„	50	6 22 20	„	Poor	Extensive caseo-calcareous lesions in bronchial and mediastinal glands and lungs
676	6 11*20	„	—	—	—	Emaciated	Generalised
653	6 6*11	„	—	—	—	„	„
655	5 14*15	„	50	5 9 12	„	Killed in extremis	„
673	7 20 20	„	50	7 7*13	„	Fair	Not done
668	4 5* 5	Negative	—	—	—	Emaciated	Lung cavities containing pus. Caseo-calcareous lesions in bronchial and mediastinal glands
698	6 17 16	Positive	16	5 11*18	Positive	Emaciated T.B. Udder	Not done
700	6 12 11	„	16	6 14*17	„	Emaciated T.B. Udder	„ „
709	5 20 18	„	16	4 9*13	„	Emaciated Killed in extremis	Generalised
680	6 21 15	„	27	6 10*15	„	Poor (T.B. lungs)	Not done
666	5 13 12	„	6	5 14 23	„	Fair	„ „
675	6 16 15	„	27	6 12*12	„	Poor (T.B. lungs)	„ „
665	4 20 25	„	6	5 16 10	„	Fair	„ „
659	4 12 12	„	—	—	—	Poor	Extensive caseous lesions in mesenteric glands
678	6 15 16	„	6	7 12*25	Positive	„	Not done
660(1)	7 11 24	„	7	7 12*18	„	„	„ „
(2)	7 12 13	„					
(3)	7 12 12	„					
662(1)	5 13 18	„	7	5 12 12	„	„	„ „
(2)	5 8 14	„					
(3)	5 10 18	„					
664(1)	7 7 7	Negative	—	—	—	Emaciated	„ „
(2)	7 10 16	Positive					
670	5 20 23	„	—	5 16 12	Positive	Poor	Extensive cavities in lungs containing pus

PI = pre-injection measurement of skin.
48 = measurement of skin at 48th hour.
72 = measurement of skin at 72nd hour.
* = given 2nd injection at 48th hour.

CHEMOTHERAPY

By Major HAMILTON KIRK

(*Concluded*)

Sulphonamide Drugs by Local Application

Since it has become established that the sulphonamide group of drugs exert little irritant effect on the tissues, and are gradually absorbed from mucous and cutaneous surfaces, particularly if the latter are broken and inflamed, attention has been devoted to their application locally, either as an alternative to, or in support of sulphonamide therapy on classical lines by oral or parenteral administration. Consideration has been given particularly to the use of the drugs in war wounds in man, both in preventing and treating infection in the wound, and a considerable amount of evidence has been accumulated.

In the very early days the more soluble sulphonamides, such as Soluseptasine, were employed locally in the form of ointments, etc., as it was thought that their solubility would be an advantage in increasing the rate of absorption. It is now apparent, however, that a more satisfactory effect is obtained by employing relatively insoluble drugs such as sulphanilamide or sulphathiazole in the form of powder, paste or ointment, applied to a surface, or implanted in a wound.

The effect of this is the gradual absorption of the drug over a period of time so that frequent dressings are not required, and a concentration in the tissue surrounding the localised infection, sufficient to exert the appropriate bacteriostatic effect, is obtained.

It has been shown experimentally that comparable quantities of sulphanilamide, sulphapyridine and sulphathiazole, when implanted in wounds, are absorbed at a rate in direct proportion to their solubility in water, and the time taken for complete absorption of an implant has been shown experimentally by Hawking[13] to be of the order of 24 hours in the case of sulphanilamide, four or five days sulphathiazole, and seven to ten days with sulphapyridine.

Local application of the sulphonamides is now accepted as being of definite value in preventing infection in wounds. With regard to treatment, on the other hand, it became evident that the anti-bacterial effect of the drugs was seriously inhibited by the presence of pus, and experiments have shown that the presence of peptone in the culture medium has the same effect in limiting the activity of the drug. This is no doubt connected with the antagonistic effect of p-amine benzoic acid on the sulphonamides. This explains the relative inefficiency of the sulphonamides in certain localised infections in which pus formation is profuse.

Several reports have now been published on the use of sulphanilamide locally in a number of conditions commonly encountered in veterinary practice. This drug is particularly effective in the case of streptococcal infections.

Sulphathiazole is superior to sulphanilamide in being more active, particularly against staphylococcus aureus, and on the anærobic organisms, and in being absorbed somewhat more slowly. Sulphapyridine is also effective, but in certain conditions its insolubility renders it too slowly absorbed.

Apparently there is no fear of toxicity from local applications, whether the agent used is a powder, ointment or solution.

Swann[16] suggests two prescriptions for home-made pastes, viz.:

℞ Sulphanilamide powder (5%).
Zinc oxide.
Liq. Paraffin āā p. æ.
Ft. pasta.

Or another in which the zinc is replaced by iodoform. He considers it is more successful to employ the drug in solid form, ointment or suspension, rather than actual solution, in that the latter favours a too rapid absorption from the site of infection for the bacteriostatic effect of the drug to be obtained to its full advantage.

For further information on this subject, readers may care to refer to the references at the foot of the page.*

ENTOZON (Zonin).—A finely-granulated yellow substance readily soluble in water which, it is claimed, possesses very powerful bactericidal properties—even in great dilution. For instance, bacteriological experiments have shown that tissues infected by the following organisms are sterilised *in vivo* by the following dilutions:

Bac. Coli by 1 : 1,000 to 1 : 10,000 solutions.
Staphylococci by 1 : 50,000 solution.
Streptococci (hæmolytic) by 1 : 100,000 solution.

The use of higher concentrations is rarely justified. Entozon solution, having no irritant action, can be injected into the vagina or uterus in all species of animals.

Clinical indications in small-animal practice are endometritis, pyometra, vaginitis, sepsis, abscesses, etc. Some practitioners prefer to use the pliable Entozon bougies, which can be introduced into narrow apertures or cavities, such as punctured wounds or fistulæ.

In balano-posthitis of dogs, Entozon rods are especially suitable for introduction into the preputial sac.

RIVANOL (Acrolactine).—This exerts a specific bactericidal effect on pus-forming cocci. It does not coagulate albumin and therefore penetrates deeply. A solution of 1 : 1,000 is used for infected wounds; or the dusting powder may be substituted. An ointment is prepared for ocular use.

ACRIFLAVINE.—An orange-coloured antiseptic with a powerful bactericidal action which is actually enhanced in the presence of serum.

It is a most excellent, non-irritating, odourless, non-toxic drug for the treatment of wounds and general septic conditions. Obtainable in powder, tablet, solution (1 : 1,000) or pessary form.

As an emulsion with liquid paraffin, the author has proved it of exceptional value in veterinary practice. Copiously applied to wounds which have to be bandaged, it not only prevents sepsis but also prevents the dressing from sticking to the wound. This obviates the use of water, which in so many cases induces secondary hæmorrhage and which from other points of view is often undesirable.

There is a good deal of reliable evidence, apart from the author's own

* "Sulphapyridine Therapy in Local Infections." Bryan. *Jnl. A.V. Med. Ass.* Jan., 1942. Page 73.
"Trauma; A Problem of Small-Animal Practice." Millar. *Jnl. A.V. Med. Ass.* Feb., 1942. Page 165.

personal observations, that whilst the acute general infections under review should be treated by the internal administration of the sulphonamide drugs, local lesions can probably be successfully combated *only* by topical applications, which ensure a high concentration at the actual seat of bacterial activity.

Chemotherapeutics Having Anti-Protozoal Activity

Neoarsphenamine (Neosalvarsan, N.A.B., Neokharsivan)

Specific in avian spirochætosis, and enterohepatitis (Blackhead) in turkeys. It is also used to some extent in trypanosomiasis, particularly dourine in horses, although some authorities do not regard it as a completely satisfactory cure. It has been claimed to be of some value in Stuttgart disease of dogs, but there is no reliable evidence that this is so.

It is probable that its value in many febrile diseases and also in skin diseases, such as follicular mange, is due to its effect as an arsenical tonic.

Neoarsphenamine contains approximately 19 per cent. of arsenic, and is issued in ampoules on account of its great sensitivity to oxygen. After even a short exposure to air it becomes more toxic.

It is injected intravenously at blood heat. Ampoules as small as 0.15 gm. are obtainable, which is the dose suitable for a 20 lb. dog.

Turkeys, being easier to inject intramuscularly, may be given "Sulpharsphenamine" (Myosalvarsan), a slight variation of Neoarsphenamine, the dose for a 20 lb. bird being 0.1 gm. One injection usually suffices.

Acapron

A chemotherapeutic specific for piroplasmosis. In fresh infections of Babesia Canis, Acapron has a therapeutic index of 1 : 32 as against an index of 1 : 8 for drugs hitherto used in this disease. The Babesia disappear from the blood 24 hours after treatment.

In the dog, Parkin estimates the cures at 90 per cent. after a single injection. Relapses within 10 to 12 days can be cured by giving a second injection. Acapron must not be given by any other route than the subcutaneous.

Care in dosage must be exercised, as the drug is toxic in excessive amounts. The toxic effect is first to stimulate the sympathetic system and, in still higher doses, the central nervous system.

Dogs are most susceptible; then follow horses, cattle, sheep, in that order.

Subcutaneous injection of 1 mg. per kilo in cats causes salivation and contraction of the pupils. For full beneficial effect, however, the full prescribed dose must be given, which is—for dogs—¼ c.c. per 10 lb. body-weight of the 0.5 per cent. Acapron solution.

It is advisable to warn the owner of the possible by-effects, e.g., restlessness, tremors, salivation and defæcations. These symptoms can be suitably treated by subcutaneous injection of Rephrin (3-10 c.c.) according to size of animal and severity of symptoms.

Naganol

Even very small doses of this fine reddish powder have a specific action against Tryp. Evansi, the cause of Surra in dogs, cats and other animals. Its extremely high chemotherapeutic index is due to its low pharmacological efficacy and high specific action on trypanosomes.

XUM

In therapeutic doses it has no effect on the nervous or circulatory systems and produces no local irritation. It can be administered by any of the parenteral routes though the intravenous route is most effective. Accidental peri-venous injection has no harmful results.

An essential advantage of the drug is its protective effect, which lasts for weeks and even months in animals treated. The protective property of the drug results from its capacity to circulate in an active form in the body for a lengthy period through becoming fixed in the blood-stream by combination with the protein substances, particularly the albumins.

The effect of Naganol is most probably due to direct action on the trypanosomes by influencing their process of division and preventing their increase, so that they succumb easily to the defence mechanisms of the body.

A dog receives gr. $\frac{1}{2}$-$\frac{3}{4}$ per kgm. of weight as a solution in distilled water, and one injection is usually sufficient, though another may be given in eight days' time. The dose for the cat is one-twelfth gr. to one-tenth gr. per two and one-fifth lb. weight. Twenty-four hours after injection there is a fall in temperature, disappearance of hæmoglobinuria, and improvement in appetite.

Trypan Blue

Administered intravenously in a one per cent. solution to dogs suffering from piroplasmosis, the dose being 2 to 15 c.c., according to weight. Subcutaneous injection is inadvisable as causing generally some slough and abscess formation.

Diamidine Compounds

Several published reports have appeared during the last two or three years upon the efficacy of these compounds in protozoan infections.

Those of particular interest—4 : 4′ diamidino stilbene (Stilbamidine), 4 : 4′ diamidino diphenyl ether (Phenamidine), 4 : 4′ diamidino diphenoxy propane (Propamidine), and 4 : 4′ diamidino diphenoxy pentone (Pentamidine).

The activity of these compounds has been demonstrated in trypanosomiasis, leishmaniasis, and piroplasmosis; and two recent reports[17][18] have appeared on the effects of Propamidine and Phenamidine in Canine Babesiasis.

"The first work on the action of the aromatic diamidines in *Babesia Canis* infection was carried out by Lourie and Warrington Yorke[19] (1939) and they found that most of the compounds they examined had a definite action on Babesia Canis infection in puppies but that diamido diphenyl ether (phenamidine) was much less toxic, and in a dose of 10 mg. cured all five of the puppies under experiment. . . . These early experimental observations have been amply confirmed in natural cases of tick fever in dogs in Uganda. The compound has been used in 25 successive unselected cases with completely satisfactory results, in that there was no toxic reaction following the administration of the drug and there were no deaths or relapses in the dogs treated. These included several very advanced cases and one which was showing hæmoglobinuria and collapse.

The dose used is 10 mg. per kilo body-weight. Owing to the fact that Babesia Canis can readily be made resistant to these aromatic diamidines, it is important to have adequate initial dosage.

Phenamide is readily soluble in distilled water, forming a stable solution, and this is made up in rubber-capped sterile bottles of 25 c.c. in a concentration of 10 mg. in 0.5 c.c. The solution is injected subcutaneously and in this strength appears to be non-irritant. In very large dogs the dose can be divided over two injections, so as to ensure rapid and complete absorption.

The blood is negative in 12 to 24 hours and the temperature usually returns to normal within this period. Clinical improvement is rapid and uninterrupted, but in cases where anæmia is very marked hæmatinic treatment for a few days following the specific therapy is indicated.

Diamidino diphenyl ether is excellent in every way in the treatment of tick fever in

dogs and its main advantages are its specificity and therapeutic efficiency in a single dose, the absence of undesirable reactions and its low toxicity. In this respect it is a great advance on other preparations used in the treatment of Babesia Canis in dogs." (*Vet. Rec.*, *54*, 16, 158.)

The reader may wish to refer to other references, which are indicated at the foot of the page.[20][21][22]

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A NEW POLICY FOR VETERINARY SCIENCE

By SIR ALBERT HOWARD, C.I.E.

THE specialist in the diseases of livestock who reads the title of this article will wonder why the troubles which afflict crops have intruded into a journal specialising in veterinary science and largely devoted to the maladies which afflict our domesticated animals. The reason is that Nature is one and indivisible and that many of the diseases of livestock have their origin in the soil and are closely connected with the lack of quality in the crops on which these animals feed. If this point of view can be established, it follows that the basis of the veterinary practice of to-morrow must be broadened to include the whole range of husbandry, so that our livestock can be studied in relation to their environment. This means that the future veterinarian will have to take a much wider sweep of the subject and finally become a student of animal husbandry in the widest sense. Following our English tradition, the future veterinary surgeon will, of course, retain his old title, but the scope of his work will expand and his usefulness and standing in the farming world will improve out of all knowledge. To accomplish all this, far-reaching changes in veterinary teaching will

be necessary which will also involve a drastic reorganisation of the research work now in progress.

What evidence exists to justify an inquest on present-day teaching and research in veterinary science? What is amiss with the principles underlying our existing policy? The purpose of this article is to answer these questions, to suggest that the whole subject be reconsidered and that a new policy, based on preventing disease altogether, should take the place of current practices.

In presenting the evidence in this matter I can best begin by briefly recounting my own experience of disease in plants and livestock, which has covered a period of over forty years spent in agricultural research in many parts of the world.

I took up research in agriculture as a mycologist in the West Indies in 1899, where I specialised in the diseases of sugar-cane and cacao and became interested in tropical agriculture. Almost at once I discerned a fundamental weakness in the research organisation: the mycologist had no land on which he could take his own advice about remedies before asking planters to adopt them.

My next post was botanist at Wye College in Kent, where I was in charge of the experiments on hops and had ample opportunities for studying the insect and fungous diseases of this interesting crop. But again I had no land on which I could try out certain ideas that were fermenting in my mind about the prevention of hop diseases.

In 1905 I was appointed Imperial Economic Botanist to the Government of India. At the Pusa Agricultural Research Institute I had for the first time all the essentials for work—interesting problems, money, freedom, and, last but not least, 75 acres of land on which I could grow crops in my own way and study their reaction to insect and fungous pests and other things. My real training in agricultural research then began—six years after leaving the University and obtaining all the paper qualifications and academic experience then needed by an investigator.

At the beginning of this second and intensive phase of my training I resolved to break new ground and try out an idea (which first occurred to me in the West Indies), namely, to observe what happened when insect and fungous diseases were left alone and allowed to develop unchecked, and where indirect methods only, such as improved cultivation and more efficient varieties, were employed to prevent attack. This point of view derived considerable impetus from a preliminary study of Indian agriculture. The crops grown by the cultivators in the neighbourhood of Pusa were remarkably free from pests of all kinds; such things as insecticides and fungicides found no place in this ancient system of agriculture. I decided that I could not do better than watch the operations of these peasants, and acquire their traditional knowledge as rapidly as possible. For the time being, therefore, I regarded them as my professors of agriculture. Another group of instructors were obviously the insects and fungi themselves. The methods of the cultivators if followed would result in crops practically free from disease; the insects and fungi would be useful for pointing out unsuitable varieties and methods of farming inappropriate to the locality.

In order to give my crops every chance of being attacked by parasites,

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nothing was done in the way of prevention; no insecticides and fungicides were used; no diseased material was ever destroyed. As my understanding of Indian agriculture progressed, and as my practice improved, a marked diminution of disease occurred. At the end of five years' tuition under my new professors—the peasants and the pests—the attacks of insects and fungi on all crops, whose root systems were suitable to the local soil conditions, became negligible. By 1910 I had learnt how to grow healthy crops, practically free from disease, without the slightest help from mycologists, entomologists, bacteriologists, agricultural chemists, statisticians, clearing-houses of information, artificial manures, spraying machines, insecticides, fungicides, germicides, and all the other expensive paraphernalia of the modern Experiment Station.

I then posed to myself the principles which appeared to underlie the diseases of plants:

1. Insects and fungi are not the real cause of plant diseases but only attack unsuitable varieties or crops imperfectly grown. Their true role is that of censors for pointing out the crops that are improperly nourished and so keeping our agriculture up to the mark. In other words, the pests must be looked upon as Nature's professors of agriculture: as an integral portion of any rational system of farming.

2. The policy of protecting crops from pests by means of sprays, powders, and so forth is unscientific and unsound as, even when successful, such procedure merely preserves the unfit and obscures the real problem—how to grow healthy crops.

3. The burning of diseased plants seems to be the unnecessary destruction of organic matter, as no such provision as this exists in Nature, in which insects and fungi after all live and work.

This preliminary exploration of the ground suggested that the birthright of every crop is health, and that the correct method of dealing with disease at an Experiment Station is not to destroy the parasite, but to make use of it for tuning up agricultural practice.

Steps were then taken to apply these principles to oxen, the power unit in Indian agriculture. For this purpose it was necessary to have the work cattle under my own charge, to design their accommodation, and to arrange for their feeding, hygiene, and management. At first this was refused, but after persistent importunity, backed by the powerful support of the Member of the Viceroy's Council in charge of agriculture (the late Sir Robert Carlyle, K.C.S.I.), I was allowed to have charge of six pairs of oxen. I had little to learn in this matter, as I belong to an old agricultural family and was brought up on a farm which had made for itself a local reputation in the management of cattle. My work animals were most carefully selected and everything was done to provide them with suitable housing and with fresh green fodder, silage, and grain, all produced from fertile land. I was naturally intensely interested in watching the reaction of these well-chosen and well-fed oxen to diseases like rinderpest, septicæmia, and foot-and-mouth disease which frequently devastated the countryside.* None of my animals was segregated; none was inoculated;

*These epidemics are the result of starvation, due to the intense pressure of the bovine population on the limited food-supply.

they frequently came in contact with diseased stock. As my small farmyard at Pusa was only separated by a low hedge from one of the large cattle-sheds on the Pusa estate, in which outbreaks of foot-and-mouth disease often occurred, I have several times seen my oxen rubbing noses with foot-and-mouth cases. Nothing happened. The healthy well-fed animals reacted to this disease exactly as suitable varieties of crops, when properly grown, did to insect and fungous pests—no infection took place.

As the factors of time and place are important when testing any agricultural innovation, it now became necessary to try out the three principles referred to above over a reasonably long period and in new localities. This was done during the next twenty-one years at three centres: Pusa (1910-24), Quetta (summers of 1910 to 1918), and Indore (1924-31).

The results obtained at these three centres, which covered a total period of twenty-one years, more than confirmed the preliminary observations described above. In one direction—virus disease—new ground was broken. This was observed on tobacco. When care was devoted to the details of growing the seed, to the raising of the seedlings and to transplanting, as well as the humus content of the soil, this disease soon disappeared and for nearly fifteen years not a single diseased plant was observed. Nothing was done in the way of prevention beyond good farming.

One significant factor was common to all these results—namely, the role of well-made farmyard manure for maintaining soil fertility, which in turn appeared to be the basis of health.

Humus and Disease Resistance

Even on the experiment stations in India the supply of farmyard manure was always insufficient. The problem was how to increase its volume and to improve its quality. The solution was suggested by the age-long practices of China. It involved the study of how best to convert the animal and vegetable wastes into humus, so that every holding in India could become self-supporting as regards manure. But such a problem did not fall within my sphere of work—the improvement of crops. It obviously necessitated a great deal of chemical work under my personal control. The organisation of research at Pusa, however, had gradually become more rigid; the old latitude which existed in the early days became a memory. That essential freedom, without which no progress is possible, had been slowly destroyed by the growth of research organisation based on fragments of science, rather than on the practical problems which needed investigation. The instrument became more important than its purpose. Such organisations, of course, can only achieve their own destruction. This was the reason why I had to leave Pusa and spend some precious years in collecting the funds to found a new centre where I should be free to follow the gleam unhampered and undisturbed. All this took six years—1918 to 1924—before the Indore Institute could be founded. In due course a simple method, known as the Indore Process of composting vegetable and animal wastes, was devised, tested and tried out on the 300 acres of land at the disposal of the Institute of Plant Industry, Indore. In a few years production more than doubled, the crops were to all intents and purposes immune to disease. In 1931

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the results were published by the Oxford University Press in book form under the title—*The Waste Products of Agriculture: Their Utilisation as Humus*. In this work I was ably assisted by one of my Indian staff—Mr. Y. D. Wad—the junior author of the final report.

Since 1931 steps have been taken to get the Indore Process tried out all over the world, at first by the great plantation industries—coffee, tea, sugar, sisal, maize, cotton, tobacco and rubber—and later, in farming and gardening. The results have confirmed and indeed have extended those obtained at Indore.

In 1939 an important development occurred. On March 23 of that year the *Medical Testament* of the County Palatine of Chester Local Medical and Panel Committees was unanimously adopted at a public meeting held at Crewe. In this document the dependence of the public health system of to-morrow on the fresh produce of a fertile soil was foreshadowed. Its adoption was followed by: (1) the County Garden Competition (which has done much to make Cheshire compost minded), and (2) the publication of the *News Letter on Compost*, the purpose of which is to record the growing volume of evidence that soil fertility is the basis of public health.

It soon became evident that the time had come to set out the whole humus case in such a manner that a new foundation for agricultural research could be established, which could replace the present organisation based on the fragments —the separate sciences—of a great biological complex. This took the form of *An Agricultural Testament*, which was published by the Oxford University Press in June, 1940, and reprinted two years later in June, 1942.

These various publications have led to important developments overseas, notably in South Africa, New Zealand and the United States of America, in all of which new ground is being constantly broken. The progress made can be followed by consulting the following three periodicals:

(1) *The Farmer's Weekly* of South Africa (P.O. Box 387, Bloemfontein, S.A.).

(2) *The Compost Club Magazine* of New Zealand (P.O. Box 1303, Auckland, N.Z.).

(3) *Organic Gardening and Farming* (The Rodale Press, Emmaus, Pa., U.S.A.).

The Mycorrhizal Association and Disease

Why is humus the basis of disease resistance and of fertility in the crop and also in livestock? The circulation of protein in Nature and the mycorrhizal association provide the clue.

Let us first consider the significance of the circulation of protein. The first stage in this process is the synthesis of humus from vegetable and animal wastes through the agency of fungi and bacteria. Humus results from the amalgamation of the undecomposed portions of the vegetable and animal wastes of a properly assembled and properly managed compost heap, and the dead bodies of the fungi and bacteria which ferment these wastes. Such humus can be looked upon as the first segment of the wheel of life. In the soil this humus undergoes two very different series of changes: (1) a portion is mineralised by

the soil organisms with the formation of the salts needed for the work of the green leaf; (2) some of the remainder nourishes certain soil fungi which invade the active roots of the crop and live therein in partnership with the plant. Eventually the fungous threads of this mycorrhizal association are digested by the plant, by which means proteins pass from the soil to the green cells of the leaf. The first step in the circulation of protein in Nature is thus accomplished. The next step in this circulation by means of animal and human digestion is so well understood that it needs no argument. When the waste products of the animal and of the plant come together again this circulation of protein is resumed. That is what takes place in Nature—in the forest, in the prairie and in the ocean. If we copy it in our agriculture, two important consequences are realised: (1) the plant and the animal retain the fertility principle; (2) both plant and animal are able to resist the parasite. If, however, we interpose a substitution phase for the essential protein by the use of artificial manures, the power of reproduction is lost and the plant and the animal are compelled to retreat before the parasite.

One of the many examples from crop-production which can be quoted to establish this thesis is the cultivation of the vine. In the Orient this crop is always manured with farmyard manure; artificials are unknown. The consequence is that the variety does not run out. It is to all intents and purposes eternal, because each generation is grown by methods laid down by Nature. Moreover, there is practically no disease. In the West, where the crop is raised mostly on artificial manures, the variety soon runs out and insect and fungous pests have to be kept at bay by means of poison sprays.

In livestock similar results are obtained. That the nutrition of our animals is leading to difficulties in reproduction is proved by the growing incidence of the infection of the mother—mastitis, contagious abortion and other troubles associated with the breeding animal. The lowered resistance to disease is indicated by the constant reappearance of a virus trouble—foot-and-mouth disease, the occurrence of which is a sure sign that something is wrong with the circulation of protein.

How can these views of disease and its prevention be put to a crucial test? By practical experience.

In the case of crops this is now being done everywhere and the results obtained support the thesis put forward in this article. I will quote one example. A few years ago Mr. A. R. Willis, of the Tadburn Nursery, at Romsey, Hampshire, found that the use of chemicals in his tomato houses led to wilt disease. Three houses—three acres in extent—became badly infected. On my advice he composted the diseased haulms of these three acres, applied the compost to the same houses and grew a new tomato crop. This was free from disease. He then took up the Indore Process and gave up the use of artificials. His nursery has never looked back. It now enjoys a high reputation for quality and there is a great demand for the produce.

In the case of foot-and-mouth disease a similar crucial experiment is needed. A cattle farm should be first put in order by means of freshly prepared humus and a breed which suits the locality should then be got into good fettle by

means of produce raised on the farm. A few mild foot-and-mouth cases should then be allowed to run with the herd. Two things are likely to happen. The affected animals will soon recover and the herd will either escape infection altogether, or if a few cases develop, they will rapidly cure themselves. Similar results will be obtained in such troubles as mastitis, contagious abortion, Johne's disease, tuberculosis and so forth.

When these results are obtained the veterinarian of the future will be in a position to make use of the diseases of livestock to test farming practice. If the introduction of a diseased animal on a farm leads to no new cases, then all is well with the methods employed. If infection does take place, then a case for the complete overhaul of the methods of agriculture is called for.

It follows from the above that the current proposals for the control of animal diseases by orthodox methods, such as the direct assault on the parasite, or its avoidance, by vaccines and sera, are bound to fail, because they are based on the wrong principles. All these troubles are messages from Mother Earth that things are not well. We must, therefore, give the right answer to these messengers of Nature; the underlying causes of the despatch of these missives must be removed. This can only be done by the methods above indicated—the restoration and maintenance of soil fertility, so that the food of the animal is properly constituted. This must be followed by good management.

So much for future policy. What is to be done while our inheritance—the soil of the island in which we are living—is being restored to us? How are we to liquidate the vested interests—professional, administrative and commercial—which are firmly established along our path?

As far as veterinary practice is concerned, a dual policy must be pursued—the present methods will have to be continued, but with more and more modifications in the direction of prevention. Eventually preventive methods will replace the idea of direct control.

The elimination of the various vested interests can, in my judgment, be achieved only in one way—by arranging matters so that Mother Earth herself gives the verdict in the suits—"humus versus artificials" and "humus versus a combination of the two." The procedure that must at all costs be avoided is to attempt to settle these problems by discussion and argument. This will only lead to infructuous disputations between the lawyers on either side. But if the question is properly posed to Mother Earth, her verdict will be so clear and definite that nothing more need be said.

How can this matter be put to Mother Earth in such a manner that both sides can get a square deal? In a very simple way. Arrangements must be made for two farms to be run side by side, one based on the law of return, the other on the use of artificial manures. In both farms the crops and the breeds must be raised from seed or animals fed on the local produce. In this way the cumulative effect of the soil on the crop—plant and animal—will be recorded.

Such a test is already in progress at New Bells Farm, Haughley, near Stowmarket, in Suffolk. An account of Lady Eve Balfour's scheme will shortly appear in book form. I sincerely commend it to all members of the veterinary profession.

Abstracts

THE TREATMENT OF SHOCK IN THE DOG*

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WHEN we consider a disease entity, the first thing that we consider is its definition; the second thing that we consider is its etiology. In regard to the subject of shock, it is difficult to agree on a definition of the condition. The reason for this is that some attempt to define shock on an etiologic basis. Others attempt to define it on a symptomatic basis.

If I had an animal that was in shock and would show the animal to you, I believe that every one of you would agree with the statement that the animal is in shock. The reason for the agreement is that we have in our minds a symptomatic definition of shock. The same is true with the human patient—physicians and surgeons do not have difficulty in agreeing when a patient is in shock. The animal or the patient is in a state of collapse, the blood pressure is low, and the pulse is weak, thready and rapid. The reflexes are very much depressed or may be absent. The animal or the patient may be unconscious but may be aroused with effort. The patient may not be in complete coma. In the case of the human patient, the skin is pale, cold and clammy. When we have a picture of that sort presented to us, we say that the patient is in shock.

The reason why we cannot agree on an etiological definition of shock is because, at the present time, we do not know its etiology. For some reason or other the circulation has been markedly embarrassed, so that there is a stasis of blood at the periphery. The exact cause of this, in all conditions that lead to shock, we do not know. We know that if this peripheral stagnation continues for a sufficient length of time, there will be a fall in the blood pressure because of decreased venous return to the heart; there will be a decrease in the pulse pressure and the cardiac output, and an increase in heart rate for the same reason. The heart does not have enough blood returning to it to be pumped out to maintain the blood pressure, to maintain the pulse pressure, and to maintain a slow heart rate.

Hemoconcentration and a decrease in blood volume follows or is associated with peripheral stagnation. This is due to what we call exemia, or the passage of blood plasma into the tissue spaces.

After the blood pressure has been reduced to the shock level, that is, to 40 or 50 millimetres of mercury systolic pressure, and has remained there for a period of two to three hours, in our experience we have never been able to resuscitate the animal. Dr. Wiggers,[1] in a recent review of the subject of shock, defines shock as a condition in which there is a decrease in blood volume, an hæmoconcentration and a decrease in the blood pressure, and from which the animal cannot be resuscitated. In other words, he goes as far as to say that he cannot absolutely diagnose shock in the animal until it is in a condition from which it is sure to die.

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I prefer to define shock symptomatically; and in so far as the response to therapy is concerned, I prefer to consider that there are different degrees of shock. There is a degree of shock that responds to simple therapy. There is a second degree that requires more vigorous therapy (repeated transfusions). And then, finally, we reach a degree of shock from which the patient cannot be revived.

This morning I want to tell you about our observations on three different types of shock which we have been studying: First, shock or death, which results from loss of blood not involving trauma, such as lacerations of large arteries, sometimes called "hæmorrhagic shock." Second, the type of shock that we have to deal with in a fracture of a limb, associated with hæmorrhage and seeping of blood and plasma into the surrounding area of bruised tissue—"traumatic shock." And, third, "post-operative shock."

Hæmorrhagic Shock

How much blood can an animal lose and still survive? This question has never been answered adequately by actual evidence, so an experiment was performed to provide this information. Under local anæsthesia the carotid artery of the dog was exposed, the head end of the artery tied off, a glass cannula was introduced into the heart end of the artery, and the animal was permitted to bleed as much as it would through the cannula. Bleeding stopped in from seven to 15 or 20 minutes. During that period of time they lost from 45 to 67 per cent. of their total blood volume. It is remarkable that 15 per cent. of the dogs survived an extensive hæmorrhage of that sort. However, there is quite a wide variation. Some dogs die when they lose 45 per cent., that is, about one-half of their blood volume; other dogs die only after losing two-thirds of their blood volume, or 66 per cent., and some will survive the loss of even two-thirds of their blood volume.

That means: a dog can suffer a relatively severe hæmorrhage, a large artery or vein can be sectioned, and if the animal does not die rapidly, there is a chance that we can save its life.

The questions arises: What is the best thing to do? The answer depends upon what we have immediately available to give the animal and also how long it has been since the hæmorrhage occurred. There has been some doubt as to whether sodium chloride solution is beneficial under these conditions. Our evidence, collected on 50 animals, shows that a number of the bled-out animals which did not die rapidly could be saved by injecting normal saline solution intravenously. The mortality of acute hæmorrhage was reduced from 85 per cent. to about 50 per cent. So if an animal that has lost a great deal of blood is brought to you, give sterile normal saline solution. It should be given in quantities of one pint, or about 500 c.c., and injected as rapidly as possible.

Why does the sodium chloride solution work as it does? The dog has 15 gm. of hæmoglobin per 100 c.c. of blood. If the animal loses two-thirds of its total blood volume it still has enough hæmoglobin to furnish a level of 5 gm. per 100 c.c. if the blood volume be brought up to normal. Five gm. of hæmoglobin per 100 c.c. in the circulating blood is adequate to maintain life. For example, we have patients with high-grade primary and secondary anæmia that

have only 5 gm. of hæmoglobin per 100 c.c. of blood. They are not dyspnœic nor do they manifest air hunger when at rest, but, if they begin to exercise, then they manifest dyspnœa. These dogs that have lost two-thirds of their blood still have enough red blood cells and hæmoglobin in their blood vessels to save their lives if these can be kept in circulation. When we give the sodium chloride we simply help to keep the remaining one-third of the blood in circulation. We give the heart some fluid to pump. That is the reason why we can reduce the mortality in acute maximum hæmorrhage by 35 per cent.

Obviously the best fluid to give an animal or a human who has lost blood is good, fresh blood. There is no substitute for fresh blood.

At the present time we hear much about blood substitutes. We performed some experiments in which we used gelatin. Gelatin is inexpensive. It is a non-allergic, non-antigenic protein that may be used instead of plasma if it is injected intravenously. We found, to our surprise, that when animals were given gelatin it did not save their lives but it caused the hæmoglobin to develop a chocolate brown colour, which is the colour of methæmoglobin. The colour of the blood, however, was due to pseudo-agglutination or clumping of the red blood cells. It was this clumping of the red cells which caused death. If an animal has not lost a lot of blood, then gelatin does not cause sufficient agglutination to be fatal.

Pectin is made from apples and from citrus fruits and a very pure preparation of citrus pectin is now available. Dr. Hartman, at the Ford Hospital in Detroit, has used pectin in a number of patients in traumatic shock or in hæmorrhagic shock and has reported very definitely beneficial results. If this is the case, it would be possible to make up a pectin solution very quickly and give it when blood is not available. At the present time, our experiments have not progressed far enough for me to cite our results in the use of either dried canine plasma or pectin.

If the animal has lost blood and is not brought to the hospital until two or three hours later, it is much more difficult to save life. If you give such an animal some saline, it will leak out of the blood vessels quite rapidly, and the blood pressure will be raised only temporarily. If the animal is given some plasma solution or a blood transfusion, the blood pressure will be raised for a longer period of time. But if the blood pressure has been at the shock level for a period of from two to three hours, the prognosis is very grave. It matters not what you give, even an ample blood transfusion will not, in our experience, resuscitate.

If the blood pressure in such a transfused animal is followed, it will rise appreciably and encouragingly for a period of half an hour—sometimes for one or two hours, after which it falls to the shock level again. If a second blood or plasma transfusion is given at this time, the blood pressure will rise again, and some of the animals that have not been in shock too long and that respond in this manner will survive. Other animals, however, after a period of a half-hour or two hours will again return to the shock level. We have tried, in animals that do not respond to a first or a second blood transfusion, vasoconstrictor drugs such as neosynephrin. In our experience with six or seven such dogs, neosynephrin has raised the blood pressure temporarily but it has had,

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under the conditions of the experiment, no permanent value. This statement is probably more dogmatic than it should be, because we have not tried the drug on a sufficiently large group of animals.

Transfusion Reactions

We have performed a great number of blood transfusions in our laboratory work for various purposes. Several years ago, when we were doing blood transfusions to ascertain if the hormone that makes the gall bladder contract is in the blood, we fed some of our animals egg yolks and cream to cause the production of the hormone. We found, to our surprise, that when the donor was fed egg yolks and cream the transfusion of the blood into a fasted recipient produced an anaphylactoid type of reaction in 70 per cent. of the transfusions. Occasionally this was so severe that the animal died and the reaction occurred even though the bloods of the animals had been cross-matched and were known to be compatible. In other words, even though the blood of the donor and that of the recipient were compatible, according to the agglutination tests, if the donor had been fed cream and egg yolks and the recipient had been fasted, the latter would manifest reaction from the transfusion. We found that if both the donor and the recipient had been fed egg yolks and cream, no reaction occurred; likewise, if both the donor and the recipient had been fasted, no reaction occurred.

This may explain some of the intergroup reactions that we seen in humans. For example, when group II blood is transfused into a group II patient, a reaction occasionally occurs. So, in giving a blood transfusion in the dog, particularly if the dog has lost a large quantity of blood, it is safer to take the blood from an animal that has had nothing to eat for about 18 hours, unless the recipient has been recently fed.

Traumatic Shock

An animal showing typical traumatic shock may be one, for example, whose leg has been injured severely without fracture of the femur. If the bone has been fractured, severe shock is likely to be present. The reason for this is that, if a fracture is present, there is likely to be more real whole-blood loss than if only the soft tissues of the thigh have been bruised.

If the soft tissues of the thigh have been bruised, some of the smaller blood vessels have been ruptured and there will be some loss of whole blood into the contused and bruised tissues. In addition, there is a seepage of plasma into the injured tissues, so that the limb swells. This constitutes a sort of internal hæmorrhage. If the blood loss into these areas is sufficient, the animal will go into shock and die unless treatment is given.

Under complete anæsthesia we have injured a limb, the nerves of which were sectioned prior to the trauma, and have found that shock occurs. Part of the pain that a conscious animal sustains from an injury will contribute to shock, but it does not appear to be the fundamental cause of traumatic shock. The lethal cause of the shock in these patients is most probably hæmorrhage and loss of plasma into the contused tissues.

Most of such animals which have lost enough blood and plasma to reduce the blood pressure to the shock level, if they have not been at this level for more than an hour, can be saved. If sodium chloride solution is injected intra-

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venously, at the end of an hour of this type of shock, the blood pressure will rise to the normal level and remain there for five, ten or fifteen minutes and then it will fall to the shock level again. This shows that the normal saline solution does not have any significant value in maintaining the blood volume in such an animal, principally because it leaks into the traumatised tissues. If the animal, after being in shock less than one hour, is given a blood transfusion, an infusion of dried dog plasma or a solution of pectin, the blood pressure will be raised and remain at the normal level, and the animal will usually recover. If the animal has been in shock for longer than one hour, in our experience, the prognosis is grave. The different degrees of shock, as described for hæmorrhagic shock, will occur; some of the animals will recover after a second transfusion and others will not, regardless of the treatment.

Post-operative Shock

We "never" see post-operative shock after operations on good, healthy dogs. We can produce it in animals, however, by handling the intestines or other viscera roughly for about 15 to 20 minutes or longer. By this time the blood pressure has fallen to shock level and remains there unless treatment, such as described for hæmorrhagic and traumatic shock, is instituted.

The mechanism behind the cause of the fall of blood pressure, when the intestines are treated roughly or handled too much, is the same as that which is concerned in the cause of shock following contusion or trauma to a limb. The plasma passes into the tissue spaces (exemia) in the splanchnic area or viscera and a decrease in the blood volume and hemoconcentration results.

Vasomotor Collapse

There is one exception to the statement that we are "never" troubled in the laboratory with post-operative shock and that exception is this: When we section both splanchnic nerves—those are the sympathetic nerves which supply the blood vessels of the intestine with vasoconstrictor impulses—or when we excise the celiac ganglia through which the nerves that supply the blood vessels of the intestine with vasoconstrictor impulses pass, then the animal not infrequently manifests the condition of shock. For example, under anæsthesia we open up the abdomen by aseptic procedure. We excise the right and left splanchnic nerves and lumbar chains and then sew up the animal. Although this is done in about 15 or 20 minutes and with ether as the anæsthetic, the animal does not always recover from the anæsthesia and unless the animal is treated early it will remain in shock and die.

What is the treatment? We inject 5 milligrams of neosynephrin or ephedrine intravenously and we leave 10 milligrams under the skin. In about five or ten minutes after this treatment the animal that has been in an unconscious state for a half-hour or an hour frequently is up and drinking water.

Sectioning the splanchnic nerves prevents the vasoconstrictor impulses from passing to the blood vessels of the intestines and the blood vessels dilate and the blood stagnates in the viscera. This is a type of "primary shock" or somewhat analogous to a fainting reaction. If a vasoconstrictor drug such as ephedrine or neosynephrin is administered—both manifest a vasoconstrictor

action of long duration—the blood vessels in the splanchnic area contract and the blood is squeezed out of the splanchnic area and goes back into the general circulation, the brain is supplied with oxygen and the animal regains consciousness.

In some animals a single injection of either of these drugs is sufficient to produce consciousness and to maintain a normal condition. But there is an occasional animal in which the ephedrine or the neosynephrin will maintain the blood pressure and the circulation in good condition for only a half-hour or so and then the effect will begin to disappear, the blood will begin to stagnate again in the splanchnic area, and the animal will die unless it receives a second treatment. Occasionally an animal requires three injections.

The response to the initial treatment with these drugs is so dramatic and striking that it is difficult by precept to get my graduate students to stay with their animals during the night or to stay awake in order to give the animals a second injection should this be necessary. The animal responds so beautifully to the first injection and it is in such good condition, for half an hour or an hour, that the student gets the idea that the animal is perfectly all right, it has come through, and it is going to remain normal. Hence he falls asleep and the animal goes into secondary shock; and if the blood pressure remains at shock level for two or three hours the animal cannot be resuscitated—neither by the administration of drugs nor by blood transfusion.

The fact that in a vasomotor collapse the restoration of the blood pressure to normal, by the use of the vasoconstrictor drug, will safe life does not mean that the use of a vasoconstrictor drug will be of benefit in the hæmorrhagic type of shock or in the traumatic type of shock in which there has been a loss of blood to the outside or a loss of blood into the tissues. I emphasise this because at one time it was believed that the administration of epinephrine, ephedrine or neosynephrin would be of value in these types of shock. These drugs are of value only in those cases in which the blood volume is relatively normal and in which the primary cause of the fall of the blood pressure is due to a withdrawal of vasoconstriction. Hence, before we use these blood-pressure raising drugs we must ask ourselves whether they are suitable for the type of shock with which we are dealing; we must actually determine whether or not the blood volume within the blood vessels of the animal is normal. If it is normal, then we can expect some result from the injection of one of the vasoconstrictor drugs. If the blood volume in the vessels is less than normal, then we cannot expect a beneficial result.

Summary

I have discussed three types of shock: (a) shock due primarily to loss of a large quantity of blood; (b) shock due to contusion or trauma; and (c) the post-operative type of shock due to excessive handling of the viscera. Then I have discussed a type of fainting reaction or a vasomotor collapse which will lead to fatal shock and death unless the tone of the blood vessels is returned to normal.

REFERENCE

(1) Wiggers, C. J.: "The present status of the shock problem." *Physiol. Rev.*, *22*, (1942), 74-123.

DYSFUNCTION OF THE OVARY*

By F. E. WALSH, D.V.M.
Ames, Iowa

STERILITY in our domestic animals is one of the major problems challenging our profession. Its importance seems to parallel the advancements that have taken place in scientific breeding and feeding. Infertility is of economic importance in all classes of livestock, especially dairy cows. The lifetime of the average dairy cow does not exceed four and one-half years; hence, maximum production is never reached. Many factors are capable of interfering with the sex life of a dairy cow. In a group of cows in the same herd a number of detrimental agents may be operating at the same time.

Barrenness, whether permanent or temporary, is usually the result of pathological changes which have taken place in the organs of reproduction caused by an infection which may or may not be specific. Factors other than micro-organisms are capable of interfering with breeding efficiency. Faulty diet or a generally improper herd management are likewise contributing causes. Conception and the production of a fœtus are the result of a chain of events, many of which are of endocrine origin. Sterility will result if a breakdown occurs anywhere in the process.

Relationship of Nutrition to Reproduction

Much data have been recorded on the effect of diet upon the normal function of the reproductive organs, but more work is needed to give a better concept of the relationship between nutrients and fertility.

During the autumn and winter of 1937-38 we had a group of 12 heifers which we intended to breed in November. They came from pasture in good condition. In the dry lot, they were given the usual grain mixture, bean hay was used as the roughage. Neither external nor internal signs of heat were evident during that period. Rectal palpation revealed non-functioning ovaries. During the latter part of February we changed the hay from bean hay to alfalfa on six of the heifers. They came in heat within three weeks, were bred, and they conceived. Unfortunately, as our supply of bean hay became exhausted about this time, the remaining heifers were given alfalfa. They too became normal. We have fed bean hay before and have fed it since and never have had a similar response. Our ration was botanically adequate, but apparently chemically inadequate. Every practitioner has had cases in which he could find nothing abnormal about a cow yet she failed to conceive even when the ration was botanically adequate. When the cow was permitted to graze on pasture during the spring she became normal and conceived. What chemicals were missing when fed in the dry lot is not known. We do know, however, that she received additional hormones in the grasses.

Symptoms of Diseased Follicles

Disturbances which arise within the ovarian tissue are usually manifested by abnormal heat periods. By rectal palpation, one may find follicles not

* Abstracted from *J.A.V.M.A.*, CI, 788, 1942. 404-410.

sufficiently developed or follicles which are over-developed. This accounts for the typoestrinism or hyperestrinism, whichever the case may be. In cases of hypoestrinism, massage of the uterus and ovaries seems to afford ample stimulant to the reproductive tract. In many instances, small doses of crude ovarian stimulating hormones should prove to be of service.

Some cows which appear well nourished as well as debilitated cows may show heat periods every 12 to 15 days. These animals, if bred, do not conceive although the reproductive organs appear normal.

If the new developing follicles are ruptured and the corpus luteum expressed, the regulatory forces of the ovaries are often re-established and the cow becomes normal.

Chronic estrus (nymphomania) is a glandular disturbance occurring in all animals. The disease has not been sufficiently studied by pathologists and endocrinologists to warrant a definite statement regarding the changes which take place during this disease.

The factors which condition a cow for the development of chronic œstrus are not known. Williams has observed the disease in calves six to eight months of age as well as older animals. Numerous observers have attributed heavy feeding as a conditioning factor. Here the question arises what constitutes exaggerated form. The sex desire may be intense in some cases; in others, heavy feeding. In our own cattle the disease does not occur frequently, and the cases as a rule are not particularly alarming. We feed a ration containing 14-15 per cent. protein with a good grade of alfalfa hay. Occasionally it occurs in cows in which the reproductive organs appear normal, the œstrus cycle regular, but following the service of the bull the heat periods become continuous. It follows in the wake of some cases of metritis as well as appearing within a few days following parturition. In our herds, these cases which occur shortly after parturition are not alarming.

During the progress of the disease changes take place in the pelvic ligaments and other pelvic structures. These changes are apparently the same as those which take place in a pregnant cow, although in many instances in an extremely mild or entirely lacking. In the pregnant cow, these changes are directly under the influence of œstrogenic substances.

The daily administration of œstrin will stimulate the uterus for a considerable period, after which metaplasia sets in with decreased vascularity and a diminishing motility of the muscles. In addition, an alteration in the normal pattern has been observed by a cystic grandular hyperplasia of the endometrium in rats, and we have observed it in cattle. Male secondary sex characters, which are frequently present, suggest that the animal is being subjected to an unusual amount of adrogenic substances.

Frie classifies chronic œstrus as: (1) that occurring with ovarian cysts; (2) that occurring without ovarian cysts; (3) that incurable by ovariotomy and therefore of extra-genital origin; and (4) that form characterised by abnormally long estral periods occurring at regular or irregular intervals.

Another possible cause of nymphomania is a dysfunction of the pineal body which is physiologically antagonistic to the anterior pituitary gland.

Treatment

Spicer treated six cows, and in addition to breaking down the cysts, he gave them potassium iodide, selecting this drug on the assumption that it has some action on all gland tissue. Five of the cows were cured. The symptom of chronic œstrus disappeared very quickly under this treatment. One feature of the treatment is that the walls of the cyst become very tough, and therefore are difficult to rupture. The first cow treated has since had four calves but on again showing symptoms of chronic estrus, they were quickly relieved by the administration of potassium iodide. The administration of the drug alone is not sufficient; the cyst must be broken down.

Williams used whole ovarian extract and the corpus luteum, adrenalin and pituitary extracts in a number of cases, but did not have outstanding success with any of them. Frequent rupturing of the cysts is the best known method of treatment.

Long and Evans in 1922 discovered that follicles could be luteinised by the administration of a crude pituitary extract. Portman cites 13 cases in cattle in which he used an anterior pituitary hormone in conjunction with rupturing the cysts, with results similar to those obtained by simple rupturing of the cysts.

We find that benefits have been derived from crude anterior pituitary extract in many cases. This treatment seems to be worthy of further trials.

Summary

(1) Bovine sterility due to disturbances of the various factors other than infection is of primary importance from an economic viewpoint as well as of academic interest.

(2) There are a large number of factors which interfere with reproduction. As some of these factors are not understood there is difficulty in planning scientific treatment and control.

(3) Temporary or permanent sterility is most frequently caused by pathological changes in the various segments of the reproductive tract due to specific or non-specific infections.

(4) Endocrinology affords a basis for explaining both normal function and dysfunction of the whole reproductive tract.

There are 37 references. Thirteen case reports are given.

Reviews

The Sanitary Inspector's Handbook: A Manual for Sanitary Inspectors and other executive Public Health Officers. Fifth Edition. (1942.) By HENRY H. CLAY, F.R.San.I., F.I.S.E., Major, R.A.M.C., Army School of Hygiene. With an Introduction by Sir W. W. Jameson, M.A., M.D., F.R.C.P. XXII +534 pages. 97 Illustrations. Demy 8vo. 18s. net. H. K. Lewis & Co., Ltd.

SIR WILSON JAMESON, Chief Medical Officer of the Ministry of Health, states in the preface:

"There is special need for a concise and accurate text-book for the use of students, and to which inspectors may refer in cases of difficulty or doubt. This need is well met by Major Clay's Handbook, and the fact that it has been found necessary to issue a new edition (the fifth) in wartime is evidence of its well-established usefulness. I had the privilege of being associated with Major Clay for eleven years in the work of the Public Health Department of the London School of Hygiene and Tropical Medicine, and I know something of the service he has rendered since in the Army School of Hygiene. His experience fits him in a very special manner to be the author of such a book."

Although primarily intended for students preparing themselves for the examination qualifying for the appointment of Sanitary Inspector, the book will prove a very convenient reference work, not only for all those engaged in Public Health activities, but for all who need information on the law and practice appertaining to a large and important part of public health work.

The book is written with an easy flow, the relevant sections from the various enactments being interspaced in such a manner that the whole book is most readable. No mean task has been performed in presenting such an amount of law in so small a compass. Were the relevant Acts and Orders published *in extenso* a volume many times larger than this book would be required for this purpose alone, yet so thoroughly has the subject been covered that, for all practical purposes, the book forms a valuable reference to the laws governing such subjects as nuisances and offensive trades, housing, lighting, heating, drainage, factories and workshops, human infectious diseases and food control.

The book can confidently be recommended to veterinary surgeons who desire information on the law and practice in connection with any of these subjects, with the exception of the section dealing with the practice—as apart from the law—of meat inspection.

The practice of meat inspection is crowded into about sixteen pages. It is necessarily very superficially dealt with and unfortunately it is unreliable in many respects. There are several text-books devoted to the subject of meat inspection and there is a special examination in meat and other foods for sanitary inspectors who wish to obtain appointments in this work, hence a more elaborate treatise on this subject is, perhaps, not necessary in such a book as this.

Handling Horses: Hints and Principles for the Training of Horses and their Riders. By Lieut.-Colonel P. D. STEWART, D.S.O., D.L., J.P. Hurst & Blackett, Ltd. Price 12s. 6d.

COLONEL STEWART has, within the compass of 126 pages, produced a book on horses which is full of most useful information and which will hold the interest of both the tyro and the expert. Even if he did not know of the Colonel's reputation as a horseman and horsemaster the reader of this book would recognise the hand of an authority whose views and opinions were the result of many years of accurate observation and great experience. Chapters three and four, which deal with the initial handling of the young horse and also

the more advanced handling, are exceptionally good. His description of long rein methods and arguments in favour of the same are convincing and will convert the greatest sceptic.

Chapter five, on "First lessons mounted," shows him to be modern in ideas and technique, and again, in chapter nine, on the art of riding, he supports his theories in such a way as to transplant the art from the sphere of rule-of-thumb or go-as-you-please to that of a science. I note that in stable management he is a supporter of the manger on the ground theory. This has much to commend it. Whoever invented the high manger could have paid little attention to anatomical structure or to the lessons to be learnt from nature. There is no doubt that ground-level feeding is the natural method and, further, it is economically correct. In one large stud it was estimated to save one pound of corn daily—no small saving in a stud of such a size. While agreeing with Colonel Stewart that the working of immature horses may lead to serious structural defects, one cannot agree that the arguments based on the study of mounted skeletons are at all conclusive. It must be remembered that such skeletons are bereft of their intervertebral discs and, further, that the poise or stance of such skeletons does not give a true picture of the horse in life. Can one imagine that Eclipse had such a poker-like neck or that Persimmon had such a straight board-like back?

In chapter twelve the theories of the author and his friend, Lynwood Palmer, on the horse's feet should not be taken too literally. If one desires to weaken a foot the best way to do so is to rasp the heels down as drastically as Palmer advises. Palmer's methods had a great vogue when first introduced, but experience has shown that there are many drawbacks. Each case should be judged on its merits. There is no doubt that individual cases do show improvement, but it would be entirely wrong to advocate the wholesale adoption of his methods. Many horses so treated may have been injured, many have lost their good action.

On page 123 it is stated that "in some horses' feet it is possible to distinguish a dividing mark on the hoof." This presumably indicates the cloven hoof at some time or other. While not disputing that the horse may have possessed more than one toe in the past, I have never seen the slightest evidence of a mark on the hoof of the modern specimen which would give support to the theory. If Colonel Stewart's horses liked to eat mouthfuls of earth it is an indication that his stable management was not all that might be desired, for this is the horse's instinctive method of correcting a mineral deficiency in the diet.

His accounts of hunting, pig-sticking, polo and racing, and the anecdotes thereon, are most intriguing. It is pleasing to note that in his arguments in support of hunting he has been logical and not made use of the familiar stupid statement that one of the main purposes of hunting is the destruction of foxes, a job which could be done much more efficiently with a shot-gun.

In dealing with cruelty of any kind, Colonel Stewart will have the support of all horsemen, but I cannot agree that the practice of putting elastic bands around a horse's penis is at all common. The results of such treatment would be so acute and severe as to be obvious to anyone, and would warrant the severest penalty. Has Colonel Stewart personal knowledge of such an incident?

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If cases have occurred they are most probably the work of some mentally affected sexual pervert.

His remarks on the working of young horses and suggestions to the Stewards of the Jockey Club are to be commended.

As in all books, one can find details which one could criticise, but taking the book as a whole it should be a most useful addition to the horseman's library. It is written in an original style; it is based on personal experience; the illustrations, photographic and diagrammatic, are excellent. I hope that Colonel Stewart may find time in the future to give us more of such delectable fare.

J. McC.

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